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         MAR 20
                 MARPAT now updated daily
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                  LWPI reloaded
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         MAR 30
                 RDISCLOSURE reloaded with enhancements
         APR 02
                  JICST-EPLUS removed from database clusters and STN
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NEWS 8
                 GENBANK reloaded and enhanced with Genome Project ID field
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                  CA/CAplus enhanced with 1870-1889 U.S. patent records
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         APR 30
                  INPADOC replaced by INPADOCDB on STN
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         MAY 01
                  New CAS web site launched
NEWS 13
         MAY 08
                  CA/CAplus Indian patent publication number format defined
NEWS 14
         MAY 14
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                  patents
         JUN 27
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                  CA/CAplus enhanced with pre-1967 CAS Registry Numbers
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         JUN 29
                  STN Viewer now available
 NEWS 21
          JUN 29
                  STN Express, Version 8.2, now available
NEWS 22
          JUL 02
                  LEMBASE coverage updated
NEWS 23
          JUL 02
                  LMEDLINE coverage updated
 NEWS 24
          JUL 02
                  SCISEARCH enhanced with complete author names
NEWS 25
          JUL 02
                  CHEMCATS accession numbers revised
NEWS 26
          JUL 02
                 CA/CAplus enhanced with utility model patents from China
NEWS EXPRESS 29 JUNE 2007: CURRENT WINDOWS VERSION IS V8.2,
               CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0jc(jp),
               AND CURRENT DISCOVER FILE IS DATED 05 JULY 2007.
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L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2007 ACS on STN

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\$$

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

CN 1H-Indole-3-acetamide, N-(3,5-dichloro-4-pyridinyl)-1-[(4-

```
fluorophenyl)methyl]-5-hydroxy-α-oxo- (CA INDEX NAME)
OTHER NAMES:
     AWD 12-281
CN
     GW 842470
CN
=> file caplus medline embase biosis
COST IN U.S. DOLLARS
                                                 SINCE FILE
                                                                 TOTAL
                                                      ENTRY
                                                               SESSION
FULL ESTIMATED COST
                                                       2.85
                                                                  3.06
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FILE 'BIOSIS' ENTERED AT 13:42:50 ON 13 JUL 2007
Copyright (c) 2007 The Thomson Corporation
\Rightarrow s 257892-33-4 or AWD 12-281
         111 257892-33-4 OR AWD 12-281
=> dup rem L2
PROCESSING COMPLETED FOR L2
           80 DUP REM L2 (31 DUPLICATES REMOVED)
=> s skin disease
     134945 SKIN DISEASE
=> s L3 and (AY<2003 or PY<2003 or PRY<2003)
'2003' NOT A VALID FIELD CODE
'2003' NOT A VALID FIELD CODE
   2 FILES SEARCHED...
'2003' NOT A VALID FIELD CODE
            36 L3 AND (AY<2003 OR PY<2003 OR PRY<2003)
=> s topical
       261595 TOPICAL
=> s L5 and L6
             5 L5 AND L6
=> d 1-5 L7 ibib abs
    ANSWER 1 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
                     2004:203704 CAPLUS
ACCESSION NUMBER:
DOCUMENT NUMBER:
                         140:229455
TITLE:
                         Combination of glucocorticoids and PDE-4-inhibitors
                         for treating respiratory diseases, allergic diseases,
                         asthma and COPD
INVENTOR(S):
                        Locher, Mathias; Hermann, Robert
PATENT ASSIGNEE(S):
                         Viatris G.m.b.H. & Co. K.-G., Germany
                        PCT Int. Appl., 26 pp.
SOURCE:
                        CODEN: PIXXD2
DOCUMENT TYPE:
                        Patent
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LANGUAGE:

German

FAMILY ACC. NUM. COUNT:

DOCUMENT TYPE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

LANGUAGE:

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PATENT INFORMATION:
     PATENT NO.
                         KIND
                                 DATE
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                                                                     DATE
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                                           WO 2003-EP8607 20030804 <--
     WO 2004019984
                         A1
                                20040311
         W: AU, BR, CA, CN, CO, CZ, GE, HR, ID, IL, IN, JP, KR, LT, LV, MD,
         MK, MX, NO, NZ, PL, SG, UA, US, UZ, YU, ZA
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE,
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PRIORITY APPLN. INFO.:
                                             DE 2002-10236688
                                                                A 20020809 <--
                                                                W 20030804
                                             WO 2003-EP8607
AΒ
     The invention relates to a novel combination of a glucocorticoid, especially
     loteprednol, and at least one phosphodiesterase-4 inhibitor
     (PDE-4-inhibitor), especially hydroxyindole-derivative
N-(3,5-dichloropyridine-4-yl)-
     2-[1-(4-fluorbenzyl)-5-hydroxyindole-3-yl]-2-oxoacetamide, for a
     simultaneous, sequential or sep. administration in the treatment of
     respiratory diseases, allergic diseases, asthma and chronic obstructive
     pulmonary diseases (COPD). Formulation of glucocorticoids and
     PDE-4-inhibitors can be prepared sep. and applied at the same time or at
     different times during the day; also combinations can be formulated.
REFERENCE COUNT:
                          10
                                THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
     ANSWER 2 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
                         2004:60309 CAPLUS
ACCESSION NUMBER:
                         140:105273
DOCUMENT NUMBER:
TITLE:
                         Topical treatment of skin diseases
INVENTOR(S):
                         Rundfeldt, Chris; Kietzmann, Manfred; Hoppmann,
                          Joachim; Baeumer, Wolfgang; Kuss, Hildegard; Hoefgen,
                         Norbert
PATENT ASSIGNEE(S):
                         Elbion AG, Germany
                         PCT Int. Appl., 48 pp.
SOURCE:
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PATENT I	NO.			KIN	D :	DATE			APPL	ICAT	ION I	NO.		,D2	ATE	
WO 2004	00692	20		A1		2004	0122	1	WO 2	003-	EP75	14		2	0030	710 <
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CODEN: PIXXD2

Patent

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English

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     EP 1531818
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                                            NO 2005-718
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PRIORITY APPLN. INFO.:
                                             US 2002-395221P
                                                                 Ρ
                                                                    20020711 <--
                                             WO 2003-EP7514
                                                                 W
                                                                    20030710
OTHER SOURCE(S):
                         MARPAT 140:105273
     The present invention relates to a method for the treatment of an
     inflammatory and/or allergic skin disease comprising topically
     administering a substituted hydroxy indole which is a phosphodiesterase 4
     inhibitor. Examples are provided of the topical effectiveness
     of AWD 12-281 and cilomilast in dermal
     immunol. inflammation.
REFERENCE COUNT:
                               THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
     ANSWER 3 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:
                         2002:495906 CAPLUS
DOCUMENT NUMBER:
                         138:117605
TITLE:
                         Effects of the phosphodiesterase 4 inhibitors SB
                         207499 and AWD 12-281 on
                         the inflammatory reaction in a model of allergic
                         dermatitis
AUTHOR(S):
                         Baumer, Wolfgang; Gorr, Gilbert; Hoppmann, Joachim;
                         Ehinger, Andreas M.; Ehinger, Britt; Kietzmann,
                         Manfred
CORPORATE SOURCE:
                         Toxicology and Pharmacy, Department of Pharmacology,
                         School of Veterinary Medicine, Hanover, 30559, Germany
SOURCE:
                         European Journal of Pharmacology (2002),
                        446(1-3), 195-200
                         CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER:
                         Elsevier Science B.V.
DOCUMENT TYPE:
                         Journal
LANGUAGE:
                         English
     The inhibitors of the phosphodiesterase 4, SB 207499 (cilomilast,
     c-4-cyano-4-(3-cyclopentyloxy-4-methoxyphenyl)-r-L-cyclohexane carboxylic
     acid) and AWD 12-281 (N-(3,5-dichloropyrid-4-
     yl)-[1-(4-fluorobenzyl)-5-hydroxyindole-3-yl]glyoxylic acid amide) were
     tested in a model of allergic dermatitis in mice. To obtain an allergic
     dermatitis, BALB/c mice were sensitized to toluene-2,4-diisocyanate.
     allergic reaction was challenged by topical administration of
     toluene-2,4-diisocyanate onto the mice ears. Before challenge, two groups
     of mice were treated topically (ear skin) with SB 207499 or AWD
     12-281. There was a significant ear swelling in
     toluene-2,4-diisocyanate-challenged mice ears 4, 8, 16, 24 and 48 h after
     challenge. SB 207499 and AWD 12-281
     inhibited this swelling significantly 8, 16, 24 and 48 h after the
                For biochem. parameters and histol., ears were sampled from
     mice sacrificed 4, 8 and 16 h after the challenge. In homogenized tissue,
     SB 207499 and AWD 12-281 inhibited
     significantly the secretion of interleukin 1\beta induced by
     toluene-2,4-diisocyanate 4 and 8 h after challenge. The cell influx
     (granulocytes) observed in the toluene-2,4-diisocyanate-challenged mice 8 and
     16 h after challenge was nearly abolished by AWD 12-
```

281 and SB 204799.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:420229 CAPLUS

DOCUMENT NUMBER: 138:18980 TITLE: AWD 12-281

Kuss, H.; Hofgen, N.; Egerland, U.; Heer, S.; Marx, AUTHOR(S):

D.; Szelenyi, I.; Schupke, H.; Gasparic, A.; Olbrich, M.; Hempel, R.; Hartenhauer, H.; Krone, D.; Berthold,

K.; Kronbach, T.; Rundfeldt, C.

CORPORATE SOURCE: Arzneimittelwerk Dresden GmbH, Radebeul, D-01445,

Germany

SOURCE: Drugs of the Future (2002), 27(2), 111-116

CODEN: DRFUD4; ISSN: 0377-8282

PUBLISHER: Prous Science

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

A review. Airway diseases such as bronchial asthma and chronic obstructive pulmonary disease (COPD) are chronic inflammatory diseases whose prevalence is increasing. Current research concerned with developing effective treatments for these conditions have focused on the search for alternatives to the standard corticosteroid antiinflammatory therapy. Selective phosphodiesterase 4 (PDE4) inhibitors have received a considerable amount of attention due to their ability to suppress the functions of several cell types involved in allergic and inflammatory disorders. The selective PDE4 inhibitor AWD 12-281 is the result of a pharmacophore-based synthesis program

wherein the optimization process was supported by ligand-based drug design methods. AWD 12-281 was selected for further development for its high affinity and selectivity for the human

PDE4 isoenzyme and due to its potent activity and excellent tolerability in models of allergic rhinitis, asthma and COPD, especially after topical treatment.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 5 OF 5 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2000413538 EMBASE

TITLE: Animal models of allergic rhinitis.

AUTHOR: Szelenyi I.; Marx D.; Jahn W.

Dr. I. Szelenyi, Pulmonary Pharmacology (BF-FP2), Meissnerstr. 191, 01445 Radebeul, Germany. CORPORATE SOURCE:

stefan.szelenyi@astamedica.de

SOURCE: Arzneimittel-Forschung/Drug Research, (2000) Vol. 50, No.

11, pp. 1037-1042. .

Refs: 44

ISSN: 0004-4172 CODEN: ARZNAD

COUNTRY: Germany

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 011 Otorhinolaryngology

> 026 Immunology, Serology and Transplantation

030 Pharmacology

037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English; German

ENTRY DATE: Entered STN: 14 Dec 2000

Last Updated on STN: 14 Dec 2000

Actively sensitized Brown Norway rats and guinea pig are useful species for studying drug effects on symptoms of experimental rhinitis. Even if not all symptoms of human rhinitis can be induced and detected in the same animal species, the predictablity of methods generally used is well

acceptable. In the present review, advantages and disadvantages of experimental methods of rhinitis will be discussed.

=> s dermal or skin

L8 1414890 DERMAL OR SKIN

=> s L3 and L8

PUBLISHER:

L9 13 L3 AND L8

 \Rightarrow d 1-13 ibib abs

L9 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2007:331227 CAPLUS

DOCUMENT NUMBER: 146:308239

TITLE: Highly selective phosphodiesterase 4 inhibitors for

the treatment of allergic skin diseases and

psoriasis

AUTHOR(S): Baeumer, Wolfgang; Hoppmann, Joachim; Rundfeldt,

Chris; Kietzmann, Manfred

CORPORATE SOURCE: Department of Pharmacology, Toxicology, and Pharmacy,

Foundation, University of Veterinary Medicine

Hannover, Hannover, D-30559, Germany

SOURCE: Inflammation & Allergy: Drug Targets (2007), 6(1),

17-26

CODEN: IADTAQ; ISSN: 1871-5281 Bentham Science Publishers Ltd.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

A review. The phosphodiesterase (PDE) 4 is the predominant cAMP degrading enzyme in a variety of inflammatory cells including eosinophils, neutrophils, macrophages, T cells and monocytes. In addition, this enzyme is expressed in non-immune cells such as keratinocytes and fibroblasts. Highly selective PDE4 inhibitors are currently under evaluation for the treatment of asthma and/or chronic obstructive pulmonary disease. Due to the broad anti-inflammatory/immunomodulatory action of PDE4 inhibitors, it has been proposed that PDE4 inhibitors might also be efficacious for skin disorders such as atopic dermatitis. Consequently, PDE4 inhibitors including cilomilast and AWD 12-281 have been tested in several models of allergic and irritant skin inflammation. These PDE4 inhibitors displayed strong anti-inflammatory action in models of allergic contact dermatitis in mice, in the arachidonic acid induced skin inflammation in mice and in ovalbumin sensitized guinea pigs. The determination of cytokines in skin homogenates revealed that both Th1 as well as Th2 cytokines are suppressed by PDE4 inhibitors, indicating an anti-inflammatory activity in both the Th2 dominated acute phase as well as the Th1 dominated chronic phase of atopic dermatitis. Due to the suppression of Th1 cytokines, activity can also be expected in psoriasis. Results of early clin. trials with both topically (cipamfylline, CP80,633) and systemically (CC-10004) active PDE4 inhibitors demonstrated efficacy in atopic dermatitis and in the case of CC-10004, also in psoriasis. AWD 12-281 (GW 842470) is currently under clin. evaluation for the topical treatment of

atopic dermatitis. Results concerning clin. efficacy of this potent and selective PDE4 inhibitor are anxiously awaited.

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 2006:1256669 CAPLUS

DOCUMENT NUMBER: 146:20293

TITLE: Novel medicament combinations for the treatment of

respiratory diseases

INVENTOR(S): Pieper, Michael P.; Schnapp, Andreas; Nickolaus, Peter

PATENT ASSIGNEE(S):

Boehringer Ingelheim International GmbH, Germany

U.S. Pat. Appl. Publ., 33pp.

CODEN: USXXCO

DOCUMENT TYPE:

Patent

LANGUAGE:

SOURCE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PA	PATENT NO.				KIND DATE			APPLICATION NO.						DATE				
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		KG,	ΚZ,	MD,	RU,	ТJ,	TM,	AP,	EA,	EP,	OA							
PRIORITY APPLN. INFO.:									EP 2005-104702					i	A 20050531			
OTHER SOURCE(S):					MARPAT 146:20293													

AB The present invention relates to new medicament combinations which contain in addition to one or more, preferably one, betamimetic, at least one anticholinergic and at least one PDE-IV inhibitor processes for preparing them and their use as pharmaceutical compns.

ANSWER 3 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

2006:365169 CAPLUS

DOCUMENT NUMBER:

144:419682

TITLE:

Pharmaceutical compositions containing

phosphodiesterase IV inhibitors and immunosuppressants INVENTOR(S): Harada, Daisuke; Kobayashi, Katsuya; Manabe, Haruhiko;

Ohshima, Etsuo

PATENT ASSIGNEE(S):

Kyowa Hakko Kogyo Co., Ltd., Japan

SOURCE:

PCT Int. Appl., 78 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

Japanese

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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WO	2006	0411:	20		A1		2006		1	WO 2	005-	JP18	854		2	0051	013	
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		GM,	ΚE,	LS,	MW,	ΜZ,	NΑ,	SD,	SL,	SZ,	ΤZ,	UG,	ZM,	ZW,	AM,	ΑZ,	BY,	
		KG,	ΚZ,	MD,	RU,	ТJ,	TM											
CA	2584	261			A1		2006	0420	(CA 2	005-	2584	261		2	0051	013	
PRIORIT	Y APP	LN.	INFO	.:						JP 2	004-	2991	04	i	A 2	0041	013	

JP 2005-113265 A 20050411 W 20051013 WO 2005-JP18854

This invention relates to pharmaceutical compns. for the prevention and AB treatment of chronic skin diseases, comprising (a) a phosphodiesterase (PDE)-IV inhibitor or a pharmacol. acceptable salt thereof and (b) an immunosuppressant, which are administered simultaneously or sep. with an interval. For example, tablets were formulated containing 2-(3,5-dichloro-4-pyridinyl)-1-(7-methoxyspiro[1,3benzodioxole-2,1'-cyclopentan]-4-yl)ethanone (PDE-IV inhibitor) 20, tacrolimus (immunosuppressant) 20, lactose 123.4, starch 20, hydroxypropyl cellulose 6, and Mg stearate 0.6 mg per tablet.

REFERENCE COUNT:

THERE ARE 113 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 - ANSWER 4 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN

113

ACCESSION NUMBER:

2006:364924 CAPLUS

DOCUMENT NUMBER:

144:398341

TITLE:

Phosphodiesterase IV inhibitor and steroid combinations for the treatment of chronic skin

disease

INVENTOR(S):

Harada, Daisuke; Kobayashi, Katsuya; Manabe, Haruhiko;

Ohshima, Etsuo

PATENT ASSIGNEE(S):

Kyowa Hakko Kogyo Co., Ltd., Japan

PCT Int. Appl., 67 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

SOURCE:

Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

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PATENT NO.
                                                   KIND
                                                                                          APPLICATION NO.
                                                                  DATE
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          WO 2006041121
                                                     A1
                                                                  20060420 WO 2005-JP18855
                                                                                                                                          20051013
                  W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YIL ZA, ZM, ZW
                  SK, SL, SM, SI, IO, III, III, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, MD BH T.J. TM
                                                                                           CA 2005-2584169
          CA 2584169
                                                                  20060420
                                                     A1
                                                                                                                                           20051013
PRIORITY APPLN. INFO.:
                                                                                           JP 2004-299103
                                                                                                                                    A 20041013
                                                                                           JP 2005-113264
                                                                                                                                    A 20050411
                                                                                           WO 2005-JP18855
                                                                                                                                    W 20051013
          It is intended to provide a remedy and/or a preventive for a chronic
```

AB skin disease which comprises (a) a phosphodiesterase (PDE)-IV inhibitor or a pharmacol. acceptable salt thereof and (b) a steroid drug, which are administered simultaneously or sep. at an interval. For example, tablets were formulated containing 2-(3,5-dichloro-4-pyridinyl)-1-(7methoxyspiro[1,3-benzodioxole-2,1'-cyclopentan]-4-yl)ethanone 50, prednisolone 20, lactose 123.4, starch 20, hydroxypropyl cellulose 6, and Mg stearate 0.6 mg per tablet.

REFERENCE COUNT:

THERE ARE 128 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 5 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN 2006:226501 CAPLUS ACCESSION NUMBER:

128

DOCUMENT NUMBER: 144:267237 TITLE: The phosphodiesterase 4 inhibitor AWD 12-281 is active in a new guinea-pig model of allergic skin inflammation predictive of human skin penetration and suppresses both Th1 and Th2 cytokines in mice Hoppmann, Joachim; Baeumer, Wolfgang; Galetzka, AUTHOR(S): Christin; Hoefgen, Norbert; Kietzmann, Manfred; Rundfeldt, Chris Department of Pharmacology, elbion AG, Radebeul, CORPORATE SOURCE: D-01445, Germany SOURCE: Journal of Pharmacy and Pharmacology (2005), 57(12), 1609-1617 CODEN: JPPMAB; ISSN: 0022-3573 PUBLISHER: Pharmaceutical Press DOCUMENT TYPE: Journal English LANGUAGE: The selective phosphodiesterase 4 (PDE4) inhibitor AWD 12-281 is structurally optimized for topical administration. It has potent effects in models of lung inflammation if administered as a dry powder inhalation. It has also demonstrated its anti-inflammatory property in a mouse model of cutaneous inflammation after topical administration. The aim of this study was to evaluate whether AWD 12-281 may be capable of penetrating human skin. Therefore a new guinea-pig model of allergic skin inflammation had to be developed. In ovalbumin-sensitized guinea-pigs, intracutaneous administration of ovalbumin results in a rapid development of allergic skin wheals. Topically administered AWD 12-281 was capable of reducing the development of wheals, indicating that this compound can penetrate the stratum corneum of quinea-pig skin as a predictor of human skin penetration. A secondary aim was the evaluation of a T cell subtype preference of AWD 12-281 since PDE4 inhibitors are said to preferentially inhibit Th2-type cytokines. Therefore, the effects of AWD 12-281 on a broad spectrum of Th1- and Th2-type cytokines were studied in tissue homogenates after allergen challenge in sensitized mice and in supernatants of anti CD3/anti-CD28-stimulated peripheral blood mononuclear cells (PBMCs). In both models, AWD 12-281 suppressed both T cell subtype cytokines indicating a broad spectrum activity of AWD 12-281. A further relation of the topical activity of AWD 12-281 using a model of acute local inflammation - the arachidonic-acid-induced mouse ear edema. The compound exhibited a dose-dependent effect with a minimally

issue was to determine the duration of action and the concentration-response

effective concentration of 0.3%; after repeated administration the minimally effective concentration was 0.03%. A single administration of a 3% solution resulted in significant suppression of inflammation even 48 h after treatment. In conclusion, our results indicate that AWD 12-281 is a very promising drug candidate not only for

the treatment of lung inflammation using inhalative administration but also for the treatment of atopic dermatitis.

REFERENCE COUNT: THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS 27 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 6 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:149262 CAPLUS

DOCUMENT NUMBER: 144:239931

TITLE: Pharmaceutical compositions for the treatment of

respiratory and gastrointestinal disorders

INVENTOR(S): Jung, Birgit; Himmelsbach, Frank

PATENT ASSIGNEE(S): Boehringer Ingelheim International GmbH, Germany;

Boehringer Ingelheim Pharma Gmbh & Co. KG

SOURCE:

PCT Int. Appl., 321 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE:

OLINIA :

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

	PA	rent	NO.			KIN	D	DATE			APPL	ICAT	ION	NO.		D.	ATE	
		2006 2006						2006 2007			WO 2	005-	EP83	85		2	0050	803
		W:	ΑE,	AG,	AL,	AM,	AT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BW,	BY,	BZ,	CA,	CH,
*								DE,										
								ID,										
			LC,	LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	ΜŻ,	NA,
			NG,	NΙ,	NO,	ΝZ,	OM,	PG,	PH.,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,
			SL,	SM,	SY,	ТJ,	TM,	TN,	TR,	TT,	ΤZ,	UA,	UG,	US,	UZ,	VC,	VN,	YU,
			ZA,	ZM,	zw		,											,
		RW:						CZ,										
								MC,										
								GN,										
								NA,					UG,	ZM,	ZW,	AM,	AZ,	BY,
								TM,										
		2006																
		2575						2006									0050	
	ЕP	1784						2007								_	0050	
*		R:						CZ,										
							LU,	LV,	MC,	ΝL,	PL,	PT,	RO,	SE,	SI,	SK,	TR,	ΑĻ,
DDTA	` T M 1		•	•	MK,	YU						004		^				
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Omuri.	OWNED CONDODICAL					WO 2005-EP8385 W 2005								0050	803			

OTHER SOURCE(S): MARPAT 144:239931

AB The present invention relates to novel pharmaceutical compns. comprising at least 1 EGFR kinase inhibitor and at least one addnl. active compound selected from $\beta\text{--}2$ mimetics, steroids, PDE-IV inhibitors, p38 MAP kinase inhibitors, NK1 antagonists and endothelin-antagonists, processes for preparing the compns. and the use thereof as drugs in the treatment of respiratory or gastrointestinal complaints, as well as inflammatory diseases of the joints, the skin or the eyes. Thus, an inhalable powder contained an EGFR kinase inhibitor 150, formoterol fumarate dihydrate 50, and lactose 12,300 mg/capsule.

L9 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

2005:1155523 CAPLUS

DOCUMENT NUMBER:

143:416252

TITLE:

Novel medicament combinations for the treatment of

respiratory diseases

PATENT ASSIGNEE(S): SOURCE:

Boehringer Ingelheim International GmbH, Germany

U.S. Pat. Appl. Publ., 50 pp.

CODEN: USXXCO

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PA:	rent no.	KIND	DATE	APPLICATION NO.	DATE
DE	2005239778 102004019540	A1 A1	20051027 20051110	US 2005-109094 DE 2004-102004019540	20050419
AU	102004052987 2005235419 2559699	A1 A1	20060504 20051103	DE 2004-102004052987 AU 2005-235419	20041103 20050418
	2005102349	A1 A1 AM,	20051103 20051103 AT, AU, AZ,	CA 2005-2559699 WO 2005-EP4073 BA, BB, BG, BR, BW, BY,	20050418 20050418 BZ, CA, CH,

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CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
             LC, LK, LR, LS, LT; LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
             NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL,
             SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA,
             ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
             RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
             MR, NE, SN, TD, TG
                                20070509
                                            EP 2005-739576
     EP 1781298
                          Α1
                                                                   20050418
             AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR
    NO 2006005060
                                20061121
                                            NO 2006-5060
                         Α
PRIORITY APPLN. INFO.:
                                            DE 2004-102004019540A
                                            US 2004-578542P
                                                                Ρ
                                            DE 2004-102004052987A
                                            EP 2005-2496
                                                              A 20050207
                                            WO 2005-EP4073
                                                                W 20050418
```

OTHER SOURCE(S):

MARPAT 143:416252

GT

ΑB The present invention relates to a pharmaceutical composition comprising one or more compds. of formula I wherein n denotes 1 or 2; R1 denotes hydrogen, halogen, C1-C4-alkyl or -O-C1-C4-alkyl; R2 denotes hydrogen, halogen, C1-C4-alkyl or -O-C1-C4-alkyl; R3 denotes C1-C4-alkyl, OH, halogen, -O-C1-C4-alkyl, -O-C1-C4-alkylene-COOH, -O-C1-C4-alkylene-CO-O-C1-C4alkyl, and at least one other active substance for the treatment of respiratory diseases. The second active substance can by an anticholinergic, a phosphodiesterase IV inhibitor, a steroid, a LTD4 antagonist or an EGFR inhibitor.

ANSWER 8 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN Ĺ9

ACCESSION NUMBER: 2004:60309 CAPLUS

DOCUMENT NUMBER: 140:105273

TITLE: Topical treatment of skin diseases

INVENTOR(S): Rundfeldt, Chris; Kietzmann, Manfred; Hoppmann,

Joachim; Baeumer, Wolfgang; Kuss, Hildegard; Hoefgen,

Norbert

PATENT ASSIGNEE(S): Elbion AG, Germany

SOURCE: PCT Int. Appl., 48 pp.

CODEN: PIXXD2 Patent DOCUMENT TYPE:

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE WO 2004006920 · A1 20040122 WO 2003-EP7514 20030710

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CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
             PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
             TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                                            US 2003-611649
     US 2004038958
                          Α1
                                 20040226
                                                                     20030701
     CA 2492093
                           A1
                                 20040122
                                             CA 2003-2492093
     AU 2003254332
                           A1
                                 20040202
                                             AU 2003-254332
                                                                     20030710
     BR 2003012696
                           Α
                                 20050426
                                             BR 2003-12696
                                                                     20030710
                                 20050525
                                             EP 2003-763810
     EP 1531818
                          Α1
                                                                     20030710
             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
                          Α
                                 20051012
                                             CN 2003-821520
                                                                     20030710
                           Т
                                 20051208
                                             JP 2004-520586
     JP 2005537262
                                                                     20030710
     NZ 537482
                           Α
                                 20060929
                                             NZ 2003-537482
                                                                     20030710
     ZA 2005000108
                           Α
                                 20050223
                                             ZA 2005-108
                                                                     20050106
     NO 2005000718
                                 20050401
                                             NO 2005-718
                           Α
                                                                     20050210
PRIORITY APPLN. INFO.:
                                             US 2002-395221P
                                                                  Р
                                                                     20020711
                                             WO 2003-EP7514
                                                                  W
                                                                     20030710
                         MARPAT 140:105273
OTHER SOURCE(S):
     The present invention relates to a method for the treatment of an
     inflammatory and/or allergic skin disease comprising topically
     administering a substituted hydroxy indole which is a phosphodiesterase 4
     inhibitor. Examples are provided of the topical effectiveness of
     AWD 12-281 and cilomilast in dermal
     immunol. inflammation.
REFERENCE COUNT:
                                THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
     ANSWER 9 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
                          2003:695438 CAPLUS
ACCESSION NUMBER:
                          140:87294
DOCUMENT NUMBER:
                          AWD 12-281, a highly
TITLE:
                          selective phosphodiesterase 4 inhibitor, is effective
                          in the prevention and treatment of inflammatory
                          reactions in a model of allergic dermatitis
AUTHOR(S):
                          Baeumer, Wolfgang; Gorr, Gilbert; Hoppmann, Joachim;
                          Ehinger, Andreas M.; Rundfeldt, Chris; Kietzmann,
                         Manfred
CORPORATE SOURCE:
                          Department of Pharmacology, Toxicology and Pharmacy,
                          School of Veterinary Medicine, Hannover, D-30559,
                          Germany
SOURCE:
                          Journal of Pharmacy and Pharmacology (2003), 55(8),
                          1107-1114
                         CODEN: JPPMAB; ISSN: 0022-3573
PUBLISHER:
                          Pharmaceutical Press
DOCUMENT TYPE:
                         Journal
                         English
LANGUAGE:
     AWD 12-281 (N-(3,5-dichloro-4-pyridinyl)-2-
     [1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3-yl]-2-oxoacetamide), a
     phosphodiesterase 4 inhibitor, which is optimized for topical
     administration, was tested in a model of allergic dermatitis in mice. To
     obtain an allergic dermatitis, BALB/c mice were sensitized to
     toluene-2,4-diisocyanate (TDI). The allergic reaction was challenged by topical administration of TDI onto the mice ears. AWD \,
     12-281 was tested for its anti-inflammatory potential by
     oral, i.p. and topical administration. The phosphodiesterase 4 inhibitor,
     cilomilast (SB 207499), and/or the corticosteroid, diflorasone diacetate,
     were used as reference compds. Given orally and i.p. 2 h before as well as 5
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AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

and 24 h after TDI challenge, AWD 12-281 showed no, or only a transient inhibition of the allergen-induced ear swelling, whereas cilomilast significantly inhibited this ear swelling. Applied topically onto the ears before TDI challenge, AWD 12-281, cilomilast and diflorasone diacetate caused total inhibition of ear swelling 24 h after challenge, confirmed by a decrease of the pro-inflammatory cytokines interleukin-4, interleukin-6 and macrophage inhibitory protein-2. Administered topically after TDI challenge as therapeutic intervention, AWD 12-281 and diflorasone diacetate caused significant inhibition of ear swelling; cilomilast failed to do so. These results indicate that topically administered AWD 12-281 may be

potent in the prevention and treatment of allergic/inflammatory skin diseases.

REFERENCE COUNT:

28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 10 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

2002:495906 CAPLUS

DOCUMENT NUMBER:

138:117605

TITLE:

Effects of the phosphodiesterase 4 inhibitors SB

207499 and AWD 12-281 on

the inflammatory reaction in a model of allergic

dermatitis

AUTHOR(S):

Baumer, Wolfgang; Gorr, Gilbert; Hoppmann, Joachim;

Ehinger, Andreas M.; Ehinger, Britt; Kietzmann,

Manfred

CORPORATE SOURCE:

Toxicology and Pharmacy, Department of Pharmacology, School of Veterinary Medicine, Hanover, 30559, Germany

SOURCE:

European Journal of Pharmacology (2002), 446(1-3), 195-200

CODEN: EJPHAZ; ISSN: 0014-2999

PUBLISHER:

Elsevier Science B.V.

DOCUMENT TYPE:

Journal English

LANGUAGE:

The inhibitors of the phosphodiesterase 4, SB 207499 (cilomilast, c-4-cyano-4-(3-cyclopentyloxy-4-methoxyphenyl)-r-L-cyclohexane carboxylic acid) and AWD 12-281 (N-(3,5-dichloropyrid-4-

yl)-[1-(4-fluorobenzyl)-5-hydroxyindole-3-yl]glyoxylic acid amide) were tested in a model of allergic dermatitis in mice. To obtain an allergic dermatitis, BALB/c mice were sensitized to toluene-2,4-diisocyanate. The allergic reaction was challenged by topical administration of toluene-2,4-diisocyanate onto the mice ears. Before challenge, two groups

of mice were treated topically (ear skin) with SB 207499 or

AWD 12-281. There was a significant ear

swelling in toluene-2,4-diisocyanate-challenged mice ears 4, 8, 16, 24 and 48 h after challenge. SB 207499 and AWD 12-

281 inhibited this swelling significantly 8, 16, 24 and 48 h after $\,$ the challenge. For biochem. parameters and histol., ears were sampled from mice sacrificed 4, 8 and 16 h after the challenge. In homogenized tissue, SB 207499 and AWD 12-281 inhibited

significantly the secretion of interleukin 1β induced by

toluene-2,4-diisocyanate 4 and 8 h after challenge. The cell influx

(granulocytes) observed in the toluene-2,4-diisocyanate-challenged mice 8 and 16 h after challenge was nearly abolished by AWD 12-

281 and SB 204799.

REFERENCE COUNT:

THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 11 OF 13 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER:

2007223472 EMBASE

TITLE:

Therapeutic benefit of PDE4 inhibitors in inflammatory

diseases.

30

AUTHOR: Dastidar S.G.; Rajagopal D.; Ray A.

S.G. Dastidar, Ranbaxy Research Laboratories, Department of CORPORATE SOURCE:

Pharmacology, New Drug Discovery Research, Gurgaon 122 001,

India. sunanda.dastidar@ranbaxy.com

Current Opinion in Investigational Drugs, (2007) Vol. 8, SOURCE:

No. 5, pp. 364-372. .

Refs: 101

ISSN: 1472-4472 CODEN: CIDREE

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; General Review

Immunology, Serology and Transplantation FILE SEGMENT: 026

> 037 Drug Literature Index 038 Adverse Reactions Titles

LANGUAGE: English SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 5 Jun 2007

Last Updated on STN: 5 Jun 2007

AB Intracellular levels of cyclic nucleotides are closely regulated by distinct families of PDEs, which are responsible for the breakdown and degradation of cyclic nucleotides within cells. Type 4 PDEs have the potency to modulate the release of inflammatory mediators through cAMP-dependent and -independent mechanisms. Selective targeting of PDE4 is currently being investigated as a novel therapeutic approach in the treatment of inflammation-associated respiratory diseases such as asthma and COPD. The development of several PDE4 inhibitors, including roflumilast and cilomilast, reflects the success of this approach. principle, therapeutic intervention of an inflammatory response by PDE4 inhibitors may be extended to other chronic inflammatory disease states such as psoriasis, rheumatoid arthritis and inflammatory bowel diseases (eg, Crohn's disease and ulcerative colitis). This review explores the feasibility of PDE4 inhibitors as a promising alternative for therapeutic intervention in systemic inflammation and inflammation-based disease. .COPYRGT. The Thomson Corporation.

L9 ANSWER 12 OF 13 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

2003:307114 BIOSIS ACCESSION NUMBER: DOCUMENT NUMBER: PREV200300307114

TITLE: The phosphodiesterase 4 inhibitors AWD 12

-281 and cilomilast exhibit different

effectiveness in the prevention and treatment of

inflammatory reactions in a model of allergic dermatitis. Baeumer, W. [Reprint Author]; Hoppmann, J.; Tschernig, T.; Seegers, U. [Reprint Author]; Rundfeldt, C.; Kietzmann, M.

[Reprint Author]

CORPORATE SOURCE: Depts of Pharmacology, Toxicology and Pharmacy, School of

Veterinary Medicine, 30559, Hannover, Germany

SOURCE:

Naunyn-Schmiedeberg's Archives of Pharmacology, (March 2003) Vol. 367, No. Supplement 1, pp. R77. print. Meeting Info.: 44th Spring Meeting of the Deutsche

Gesellschaft fuer Experimentelle und Klinische

Pharmakologie und Toxikologie and the 20th Meeting of the

Gesellschaft fuer Umwelt-Mutationsforschung. Mainz,

Germany. March 17-20, 2003. ISSN: 0028-1298 (ISSN print).

DOCUMENT TYPE: Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 2 Jul 2003

Last Updated on STN: 2 Jul 2003

ANSWER 13 OF 13 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on

STN

AUTHOR(S):

ACCESSION NUMBER: 2001:297031 BIOSIS DOCUMENT NUMBER: PREV200100297031

TITLE: Studies with AWD 12281 in the skin of sensitized

mice.

AUTHOR(S): Ehinger, A. M. [Reprint author]; Gorr, G. [Reprint author];

Hoppmann, J. [Reprint author]; Telser, E. [Reprint author];

Kietzmann, M. [Reprint author]

CORPORATE SOURCE: Institut fuer Pharmakologie, Toxikologie und Pharmazie,

Tieraerztliche Hochschule Hannover, Buenteweg 17, D-30559,

Hannover, Germany

SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology, (2001) Vol.

363, No. 4 Supplement, pp. R85. print.

Meeting Info.: 42nd Spring Meeting of the German Society for Experimental and Clinical Pharmacology and Toxicology. Mainz, Germany. March 13-15, 2001. German Society for Experimental and Clinical Pharmacology and Toxicology.

CODEN: NSAPCC. ISSN: 0028-1298.

DOCUMENT TYPE: Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 20 Jun 2001

Last Updated on STN: 19 Feb 2002